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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/357,737	07/19/1999	ALESSANDRO SETTE	2473.0030005/PAJ/M-M	9669

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
12/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/357,737	SETTE ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *166,168,170,177 and 247* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *166,168,170,177,247* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/09 has been entered.

2. Claims 166,168,170,177,247 are under consideration.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 166,168,170,177,247 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (US Patent 6,150,087) in view of Berzofsky et al. (US Patent 5,980,899) in view of Guo et al. Applicants arguments have been considered and deemed not persuasive.

Chien et al. teach a peptide comprising the peptide of claim 166 (see column 27, second paragraph, AA1850-1900, wherein said peptide refers to amino acids in Figure 66 (sheet 107) and wherein said peptide comprises GVAGALVAFK). Chien et al. teach

said peptide can be conjugated to tetanus toxoid (see column 26, first complete paragraph). Virtually any intact immunogenic molecule will contain at least one helper cell epitope. Chien et al. also teach a composition containing said peptide and a carrier (see column 26, first complete paragraph). Chien et al. do not teach the peptide of claim 166/168. Berzofsky et al. teach that it is desirable to identify CTL epitopes found in HCV (see column 2, fourth paragraph). Guo et al. teach that CTL recognize viral peptides complexed with MHC (see page 364, first column, last sentence continued on next page). Guo et al. teach that said peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Chen et al. teach an immunogenic HCV peptide containing GVAGALVAFK, whilst Berzofsky et al. teach that it is desirable to identify CTL epitopes found in HCV and Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position. One of ordinary skill in the art would have been motivated to create the claimed peptide to screen for HCV peptides which were recognized by CTL because Berzofsky et al. teach that it is desirable to identify CTL epitopes found in HCV and Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position.

Regarding applicants comments and the Sette declaration, one of ordinary skill in the art would have been motivated to create the claimed peptide to screen for HCV peptides which were recognized by CTL because Berzofsky et al. teach that it is desirable to identify CTL epitopes found in HCV and Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position. Furthermore, in the post KSR Int'l Co. v. Teleflex Inc. universe, motivation per se is not even required in a rejection under 35 USC 103. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

In addition, is noted that Chien et al. state:
Examples of HCV amino acid sequences that may be useful as described herein are set forth below. ***It is to be understood that these peptides do not necessarily precisely map one epitope, but may also contain HCV sequence that is not immunogenic. These non-immunogenic portions of the sequence can be defined as described above using conventional techniques and deleted from the described sequences.*** *Further, additional truncated HCV amino acid sequences that comprise an epitope or are immunogenic can be identified as described above. The following sequences are given by amino acid number (i.e., "AAn") where n is the amino acid number as shown in FIG. 66:*
Regarding applicants comments and paragraphs 37-41 of the Sette declaration, Chien et al. disclose that the cited peptide sequences **contain** HCV epitopes and that the minimal epitope sequence can be identified using routine experimentation. No evidence to the contrary has been provided. Furthermore, it is routine in the art to test large numbers of peptides to identify immunogenic peptides from a desired molecule (for example, see specification and prior art of record). For example, the Sequence listing of the instant application discloses 3683 peptides derived from HCV wherein said peptides are derived based on various MHC class I binding peptide motifs. Similarly, the art of record such as WO 94/202127 or WO 94/03205 lists thousands of different peptides derived from antigens of interest using MHC class I binding peptide motifs. WO 94/20127 states on page 6 that:
The present invention relates to the determination of allele-specific peptide motifs for human Class I MHC (sometimes referred to as HLA) allele subtypes, in particular, peptide motifs recognized by HLA-A2.1 alleles. These motifs are then used to define T cell epitopes from any desired antigen, particularly those associated with human viral diseases, cancers or autoimmune diseases, for which the amino acid sequence of the potential antigen or autoantigen targets is known. Epitopes on a number of potential target proteins can be identified in this manner. Examples of suitable antigens include prostate specific antigen (PSA), hepatitis B core and surface antigen$_s$ (HBVc, HBVs) hepatitis C antigens, Epstein-Barr virus antigens, melanoma antigens (e.g., MAGE-I),

human immunodeficiency virus (HIV) antigens and human papilloma virus (HPV) antigens.

It is also noted that there are only a small number of peptides encompassed by the motif taught by Guo et al. Guo et al. teach that CTL recognize viral peptides complexed with MHC and that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position, wherein a routineer would have identified such peptides as potentially pertinent to the antiHCV response in HLA-Aw68 positive patients.

In fact, as per paragraph 24 of the Sette declaration, a mere 60 possible peptides are encompassed by the motif disclosed by Guo et al. This is contrast to the 3683 peptides disclosed in the instant specification wherein the vast number of said peptides are described solely with respect to binding various MHC class I alleles. The occurrence of other alleles is not germane to the instant rejection because the instant rejection provides motivation to derive peptides which could be used to treat HLA-Aw68 positive patients.

Regarding applicants comments about HLA-Aw68, one of ordinary skill in the art would have been motivated to derive peptides which bound HLA-Aw68 to treat HLA-Aw68 positive patients. Whilst there are also other HLA class I alleles that are more popular, this does not negate the need to treat HLA-Aw68 positive patients with HCV. Applicants arguments are analogous to arguing that it would not be obvious to treat a patient with a rare disease because many common diseases also occur.

Regarding applicants comments about Berzofsky et al., the Chien et al. reference discloses that the sequence comprising GVAGALVAFK contains a HCV epitope (see column 27, first paragraph). Regarding Berzofsky et al. and NS5, Berzofsky et al. does not teach that NS5 provides the only CTL epitope in HCV. Berzofsky et al. indicate that CTL epitopes would be present in other regions of HCV (for example see column 13, first paragraph and column 12, second paragraph). Regarding applicants comments about Guo et al. and 9mer peptides, said comment is made regarding the prior art. It is not a comment regarding the results disclosed by Guo et al. Guo et al. teach that peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position (see abstract).

Regarding applicants comments about “inherency” and the alleged unexpected properties of the peptide of claim 166, the MPEP section 2145 (II) states:

II. ARGUING ADDITIONAL ADVANTAGES OR LATENT PROPERTIES
Prima Facie Obviousness Is Not Rebutted by Merely Recognizing Additional Advantages or Latent Properties Present in the Prior Art
Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979) (Claims were directed to grooved carbon disc brakes wherein the grooves were provided to vent steam or vapor during a braking action. A prior art reference taught noncarbon disc brakes which were grooved for the purpose of cooling the faces of the braking members and eliminating dust. The court held the prior art references when combined would overcome the problems of dust and overheating solved by the prior art and would inherently overcome the steam or vapor cause of the problem relied upon for patentability by applicants. Granting a patent on the discovery of an unknown but inherent function (here venting steam or vapor) "would re-move from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art." 596 F.2d at 1022, 201 USPQ at 661.); In re Baxter Travenol Labs., 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991) (Appellant argued that the presence of DEHP as the plasticizer in a blood collection bag unexpectedly suppressed hemolysis and therefore rebutted any prima facie showing of obviousness, however the closest prior art utilizing a DEHP plasticized blood collection bag inherently achieved same result, although this fact was unknown in the prior art.).
"The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." Ex parte Obiaya, 227 USPQ 58, 60 (Bd. labyrinth heaters to maintain the samples at a uniform temperature. Although appellant showed an unexpectedly shorter response time was obtained when a labyrinth heater was employed, the Board held this advantage would flow naturally from following the suggestion of the prior art.). See also Lantech Inc. v. Kaufman Co. of Ohio Inc., 878 F.2d 1446, 12 USPQ2d 1076, 1077 (Fed. Cir. 1989), cert. denied, 493 U.S. 1058 (1990) (unpublished — not citable as precedent) ("The recitation of an additional

advantage associated with doing what the prior art suggests does not lend patentability to an otherwise unpatentable invention.").
In re Lintner, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990) discussed in MPEP § 2144 are also pertinent to this issue.
In addition, the peptide of claim 166 is found in the larger peptide taught by Chien et al. (associated with other naturally occurring HCV amino acids) wherein Chien et al. teach that said larger peptide is immunogenic. The MPEP section 716.02(a)[R-2] states:

Applicants must further show that the results were greater than those which would have been expected from the prior art to an unobvious extent, and that the results are of a significant, practical advantage. Ex parte The NutraSweet Co., 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991) (Evidence showing greater than additive sweetness resulting from the claimed mixture of saccharin and L-aspartyl-L-phenylalanine was not sufficient to outweigh the evidence of obviousness because the teachings of the prior art lead to a general expectation of greater than additive sweetening effects when using mixtures of synthetic sweeteners.).
The functional attributes of the peptide of claim 166 would presumably be present in the peptide of Chien et al. in that said larger peptide would be processed in vivo to yield the peptide of claim 166. The specification discloses that the peptide can be 30 amino acids long (see page 37) and conjugated to a HTL, **indicating that according to the teachings of the specification, there is no criticality regarding the length of the peptide.**
Regarding applicants comments about Yewdell et al., there is no evidence of record that suggests that the peptide taught by Chien et al. contains another immunodominant epitope that would suppress the response to the peptide recited in the claims. Applicants arguments also ignore the teachings of Guo et al. Guo et al. teach that CTL recognize viral peptides complexed with MHC (see page 364, first column, last sentence continued on next page). Guo et al. teach that said peptides which bind HLA-Aw68 generally are 9 to 11 amino acids with a V at P2 (position 2) and a K at the c-terminal position. The teachings of Guo et al. provide a reasonable expectation of

success of obtaining the claimed peptide. The MPEP section *2143.02* indicates that obviousness requires only a reasonable expectation of success.

Reasonable Expectation of Success Is Required
OBVIOUSNESS REQUIRES ONLY A REASONABLE EXPECTATION OF SUCCESS
The prior art can be modified or combined to reject claims as prima facie obvious as long as there is a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (Claims directed to a method of treating depression with amitriptyline (or nontoxic salts thereof) were rejected as prima facie obvious over prior art disclosures that amitriptyline is a compound known to possess psychotropic properties and that imipramine is a structurally similar psychotropic compound known to possess antidepressive properties, in view of prior art suggesting the aforementioned compounds would be expected to have similar activity because the structural difference between the compounds involves a known bioisosteric replacement and because a research paper comparing the pharmacological properties of these two compounds suggested clinical testing of amitriptyline as an antidepressant. The court sustained the rejection, finding that the teachings of the prior art provide a sufficient basis for a reasonable expectation of success.); Ex parte Blanc, 13 USPQ2d 1383 (Bd. Pat. App. & Inter. 1989) (Claims were directed to a process of sterilizing a polyolefinic composition with high-energy radiation in the presence of a phenolic polyester antioxidant to inhibit discoloration or degradation of the polyolefin. Appellant argued that it is unpredictable whether a particular antioxidant will solve the problem of discoloration or degradation. However, the Board found that because the prior art taught that appellant's preferred antioxidant is very efficient and provides better results compared with other prior art antioxidants, there would have been a reasonable expectation of success.).

In addition, the Yewdell et al. publication is published after the effective filing date of the instant invention and is therefore not germane to the state of the art at the time the invention was made. The MPEP section 2143.02 discloses:

PREDICTABILITY IS DETERMINED AT THE TIME THE INVENTION WAS MADE

Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. Ex parte Erlich, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986).

Furthermore, if the peptide recited in the claims is an actual physiologically relevant CTL epitope than the larger molecule containing said epitope must be processed in vivo to result in said peptide. In addition, the specification discloses that the peptide can be 30 amino acids long (see page 37) and conjugated to a HTL, indicating that according to the teachings of the specification, there is no criticality regarding the length of the peptide. Regarding Del Val et al. said reference refers to a peptide containing a CTL peptide and exogenous sequences not naturally found associated with the CTL peptide. The peptide taught by Chien et al. contains only naturally occurring HCV sequences. Regarding Eisenlohr et al., said reference actually teaches that flanking sequences can also positively effect the presentation of an immunogenic peptide (se page 484, first column, last paragraph). There is no evidence of record that addresses the effect of the flanking sequences found in the peptide disclosed by Chien et al. Furthermore, the specification, page 12, lines 15-22 indicates that the peptide can be of a variety of lengths that are longer than the actual size of the peptide bound by HLA indicating that the inventors of the instant application did not believe that such additional amino acids would generally pose problems.

5. No claim is allowed.

6. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
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